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A study of incidentally detected carcinoma in patients operated for benign thyroid disease: Is it more common than we think?

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Abstract---Aim: In this prospective study we analysed the incidence of carcinoma in patients operated with preoperative diagnosis of benign thyroid conditions, and correlate it with risk factors for further management. Methods: A prospective analysis of 94 patients that presented to a tertiary care centre in south India and diagnosed to have benign thyroid disease that required surgical management from April 2016 to October 2017. The postoperative thyroid specimen was analysed and any evidence of malignancy was noted. These patients were further evaluated and need for further treatment was analysed based on risk factors like advanced age, male sex and size of the tumour according to AGES, AMES and MACIS scoring systems. Results: In our study, 11 out of 94 patients operated for benign thyroid disease were found to have malignancy. Thus, the incidence of occult carcinoma of thyroid was significantly higher than that of the previously published literature in India, 11.7% vs 2-7%. The most common preoperative diagnosis was that of multinodular goitre. Conclusion : The incidence of malignancy in benign thyroid specimens was high in our study, but there is a need for longer follow up, to study the biology and behavioural patterns of these probably low grade tumours. There is also a need to consider total thyroidectomy as the surgery of choice for multinodular goitre in patients who are known to have higher risk of malignancy like older males, considering that the foci of malignancy may be aggressive and the known risks involved in

reoperation/completion thyroidectomy.

Keywords---Occult thyroid carcinoma, thyroid incidentaloma.

Introduction

Occult carcinoma of the thyroid is defined as carcinoma of the thyroid gland, which is not detectable by clinical examination [1]. It may be divided into one of four categories. The first group includes patients with thyroid carcinoma incidentally found in the thyroid gland after total thyroidectomy for benign disease [2-4] or at autopsy [5-12]. The second group includes patients with incidentally detected carcinoma on imaging studies, usually ultrasonography done to investigate an unrelated condition, followed by FNAC for diagnosis. The third group consists of patients with clinically apparent thyroid carcinoma metastases, where the primary tumour is not identified before surgery, and the carcinoma is found in the final histological specimen. The fourth group consists of patients with thyroid tumours in ectopic thyroid tissue with clinical symptoms or evident metastasis [1]. The first group where cancer is found in the final histopathological examination after surgery for benign pathology is the most common of them all and is the subject of our study. There is a dearth of data regarding the incidence of occult carcinoma of the thyroid in Indian literature. We aim to look for the incidence in the Indian population by evaluating patients operated for benign thyroid disease who were found to have evidence of malignancy in the final histological specimen. Moreover, the prevalence of thyroid malignancy on autopsy specimens showed disparity in incidence from 0.01% in the USA[9] to 35.6% [8] in Finland. Hence these results cannot be extrapolated uniformly to the Indian population, thus necessitating further investigation in the Indian population.

Materials and Methods

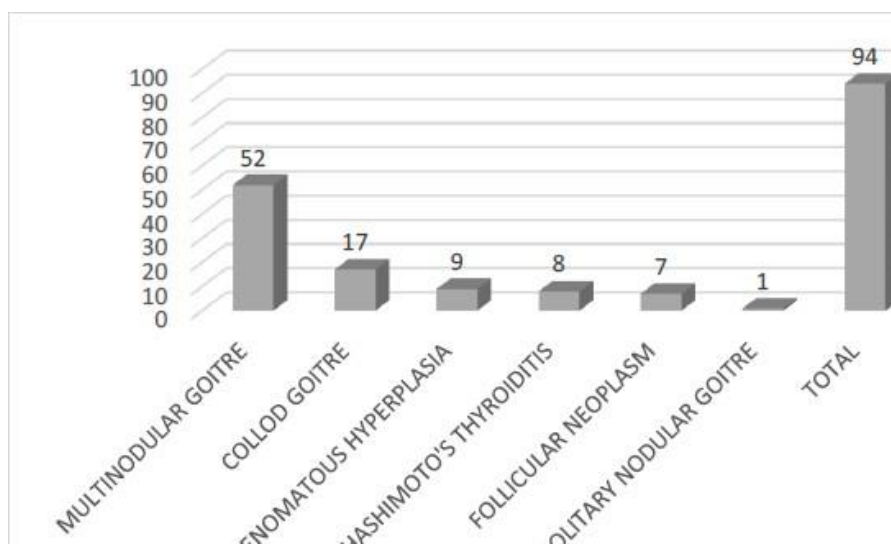
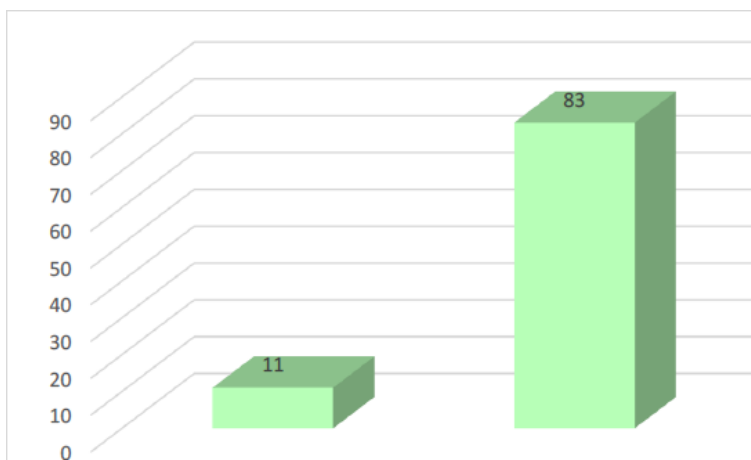
During the period covered by this study (April 2016 to October 2017), 94 patients undergoing surgery for benign thyroid disease at tertiary care centre in south India, were included. All patients underwent preoperative blood investigations, including thyroid function tests, neck ultrasound, and FNAC, and CT scan was performed only if clinically indicated. Only patients documented as having a non-malignant pathology with these preoperative investigations were included. After surgery, histopathological analysis of every thyroid specimen was performed, and evidence of occult carcinoma of the thyroid was documented. Thereafter, the demographic data of these patients, the preoperative imaging and cytological diagnosis was noted, type of surgery and follow up was recorded. The patients were then grouped as high risk or low risk based on risk stratification scores AGES, AMES and MACIS. These patients were followed up a month after surgery and followed up for recurrence or metastases every six months if the histopathological specimen was reported as malignant.

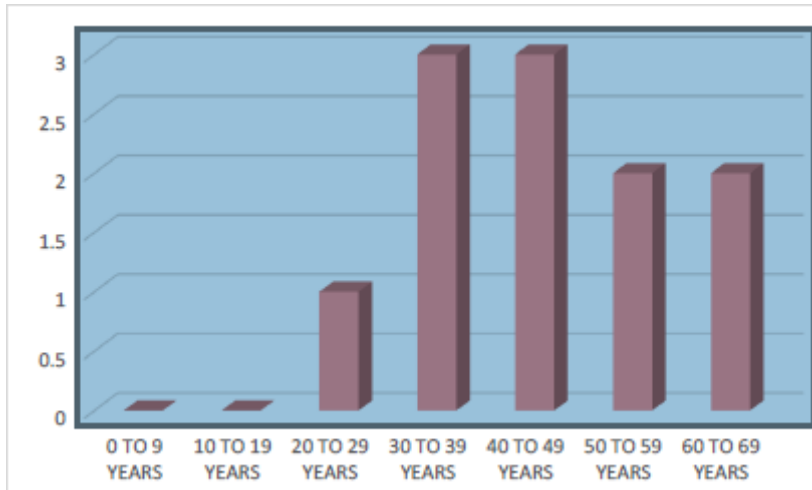
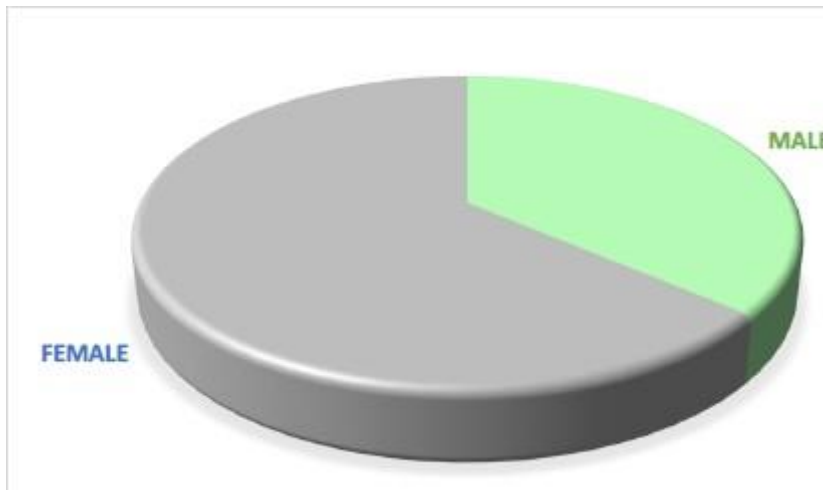
Results

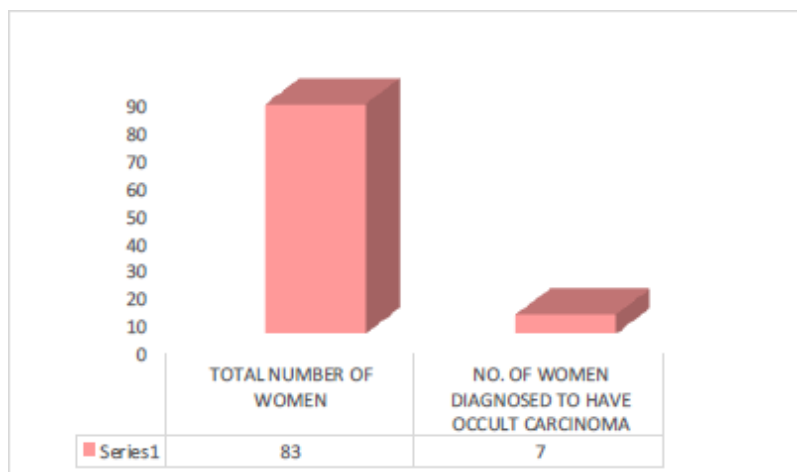
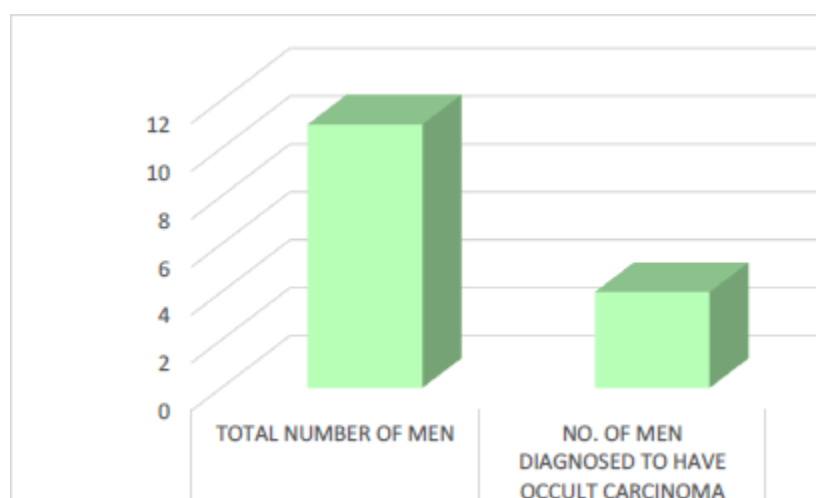
Of the 94 patients with benign thyroid disease who underwent surgical intervention, 83 were females, and 11 were males. The evaluation of the

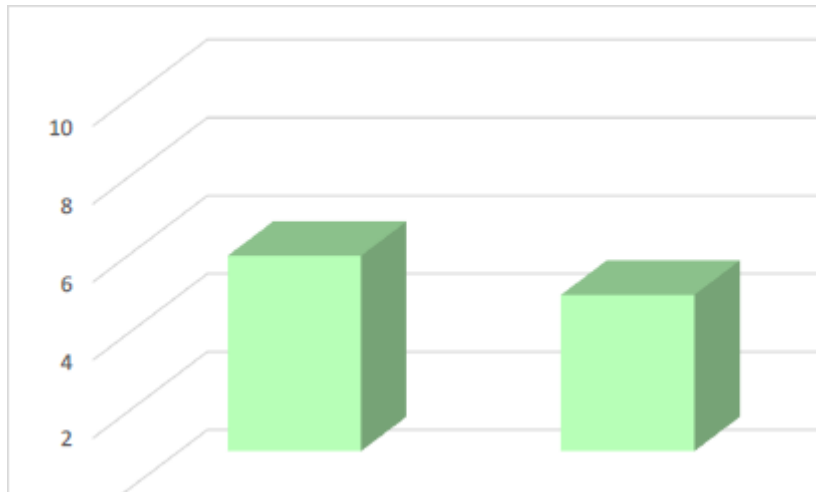
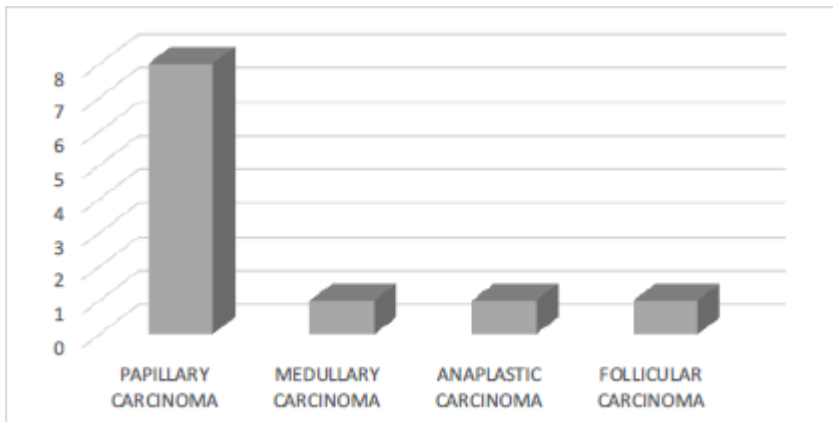
histopathological specimen revealed thyroid carcinoma in 11 patients. Thus the incidence of occult carcinoma thyroid is 11.7%. Of these 11 patients, 7 (63.6%) were female, and 4 (36.4%) were males. Thus, the incidence of occult thyroid carcinoma in females was 8.4% (7 of 83) and in males was 36.4% (4 of 11). The most common preoperative diagnosis was that of multinodular goitre, which was seen in 8 patients (72.7%), follicular neoplasm in 2 patients (18.1%) and solitary nodular goitre in 1 patient (9%). Six patients (54.5%) underwent total thyroidectomy, and five

patients (45.4%) underwent hemithyroidectomy. Of these five patients, two patients underwent a completion thyroidectomy. One of them was advised completion thyroidectomy due to a high-risk assessment score based on AGES criteria. The other patient requested to undergo a completion thyroidectomy as she was unwilling for active surveillance. The other three patients are on regular surveillance. Papillary thyroid carcinoma was more frequently observed than other malignancies, seen in 8 patients (72.7%). Of these eight patients, 3 had a classical variant (37.5%), 4 had a follicular variant of papillary carcinoma (50%), and one patient had multifocal papillary carcinoma (12.5%). Of the rest of the patients, one patient (9%) had follicular carcinoma, one patient (9%) had medullary carcinoma, and one patient (9%) had anaplastic carcinoma. The patients diagnosed to have differentiated thyroid carcinomas were assessed based on the risk assessment scoring systems MACIS, AGES, and AMES, and one patient was found to have a high risk based on the AGES scoring system. All patients are on regular follow up (mean 40 months) with imaging and plasma thyroglobulin measurements being in the normal range, showing no signs of recurrence, nodal or distant metastases at the time of completion of this study.

Graph : Preoperative diagnosis**Graph : Incidence of occult carcinoma thyroid**

Graph : Age incidence**Graph: Sex incidence in the occult thyroid carcinoma group**

Graph: Incidence of occult carcinoma thyroid in females**Graph: Incidence of occult carcinoma thyroid in males**

Graph: Type of surgical procedure**Graph: Histopathology: Postoperative diagnosis**

Discussion

The incidence of occult carcinoma of the thyroid has increased in the last three decades. The incidence probably reflects an increase in the diagnosis of asymptomatic carcinomas due to increased scrutiny and better imaging and diagnostic modalities.

There is a dearth of Indian literature regarding the incidence of occult carcinoma thyroid; the only study to our knowledge is the study conducted by Joshi et al., who analysed the post-laryngectomy specimens of patients operated for carcinoma hypopharynx and found an incidence of 2% [13]. In our series, 94 patients undergoing surgery for benign thyroid disease were evaluated. The thyroid specimen was studied for evidence of malignancy. 11 patients were found to have

incidentally detected malignancy postoperatively (11.7%). For the most part, the common preoperative diagnosis was a multinodular goitre. There are no similar studies conducted in India in a study group of patients with benign thyroid disease.

Due to the small size of the study group and the short follow-up period of three to four years, further evaluation is required to assess the significance of high incidence.

The 2015 American Thyroid Association guidelines recommend either a total thyroidectomy or a hemithyroidectomy, depending on overall thyroid status and low risk with age, personal history and family history; for thyroid cancers >1 cm and <4 cm without extrathyroidal extension and lymph node metastases. On the other hand, a total thyroidectomy was recommended for all patients with primary tumours >4 cm or with extrathyroidal extension, nodal metastatic disease, or distant metastatic disease. Patients with lateral or central neck lymph node metastases are strongly recommended to undergo neck dissections. For isolated thyroid microcarcinomas (<1cm), a hemithyroidectomy is considered sufficient [14]. Of our 11 patients diagnosed with occult carcinoma thyroid, 5 of them had already undergone total thyroidectomy for the presumed benign disease, and 2 underwent completion thyroidectomy. It may necessitate the need to reevaluate total thyroidectomy as the treatment of choice for benign thyroid disease, especially for multinodular goitre. The advantages of total thyroidectomy for benign thyroid disease include better symptom relief, lesser chance of recurrence, better postoperative control of benign disease, and in the event of the disease incidentally being discovered to be a malignancy, better diagnosis and follow up of the occult thyroid cancer. In addition, the risks of completing thyroidectomy like increased risk of bleeding, recurrent laryngeal nerve paralysis and post hypocalcaemia may be avoided. In our series, three patients had undergone hemithyroidectomy and are on regular follow up with no evidence of recurrence or metastases. Disadvantages are hypothyroidism, recurrent laryngeal nerve palsy, injury to external laryngeal nerve, wound infection, keloid formation and recurrent thyrotoxicosis

Recent studies in Japan have suggested that active surveillance may be sufficient for thyroid microcarcinomas without aggressive features. Ito et al. observed 1235 patients with micropapillary carcinoma and reported that only 8% had increased in size by 3 mm and 0.8% had nodal metastases over ten years of observation. No patients died or developed distant metastasis [15]. Another study by Oda et al. demonstrated that out of 1179 patients under active surveillance over 8 years, only 8% underwent surgery, more than half of which were

due to the patient changing their mind regarding active surveillance [16]. However, further research is needed, as there is no method to preoperatively assess which tumours will have an indolent course and which of them will have an aggressive course. In our study, one patient had a high risk based on the AGES risk assessment system, the risk factors being male sex and advanced age, and thus underwent completion thyroidectomy, but all other patients had low risk. The role of molecular markers is yet to prove their role in differentiating the high risk from the low-risk groups. As such, the patient is burdened with the

diagnosis of malignancy without well-established guidelines regarding the benefits and risks of surgical intervention as opposed to active surveillance. Hence, there is a need to formulate guidelines for the management of these incidentally detected thyroid malignancies.

Conclusion

Over the last few years, the incidence rate of occult carcinoma thyroid has dramatically increased. In this study, the incidence of occult carcinoma thyroid in patients operated for benign thyroid disease was 11.7% higher than usually reported. The highest rate was noted in the multinodular goitre group. The preoperative investigations for the diagnosis of occult thyroid carcinomas, such as ultrasound and FNAC, have demonstrated unreliable results.

Thus we propose that the only way to establish a diagnosis is by a histopathological examination of the resected thyroid specimens. The high incidence of occult carcinoma of the thyroid in our series implies the need for evaluation of risk factors that may predispose the Indian population to an increased risk. Total thyroidectomy should be considered in patients with benign thyroid disease, especially multinodular goitre, for better control of postoperative therapy, avoiding the risk of recurrence and completion of thyroidectomy, with its known technical difficulties and increased risk of complications. It also helps to diagnose and resect all possible foci of occult thyroid carcinoma, which can rarely be aggressive.

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